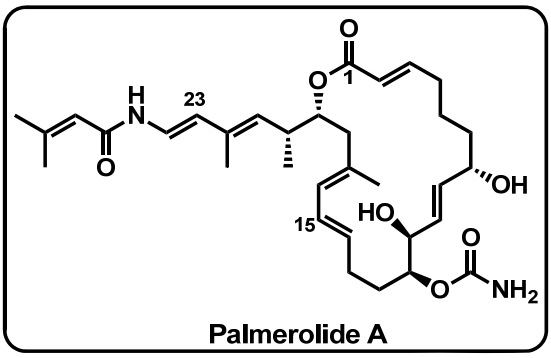
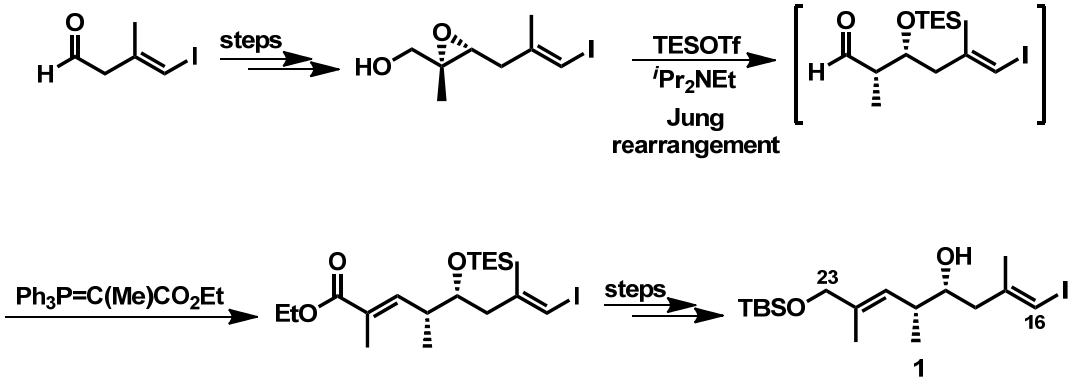
SYNOPSIS

The thesis entitled *"**Total synthesis of palmerolide A, dihydroconduritols and lentiginosine**"* is divided into two chapters.

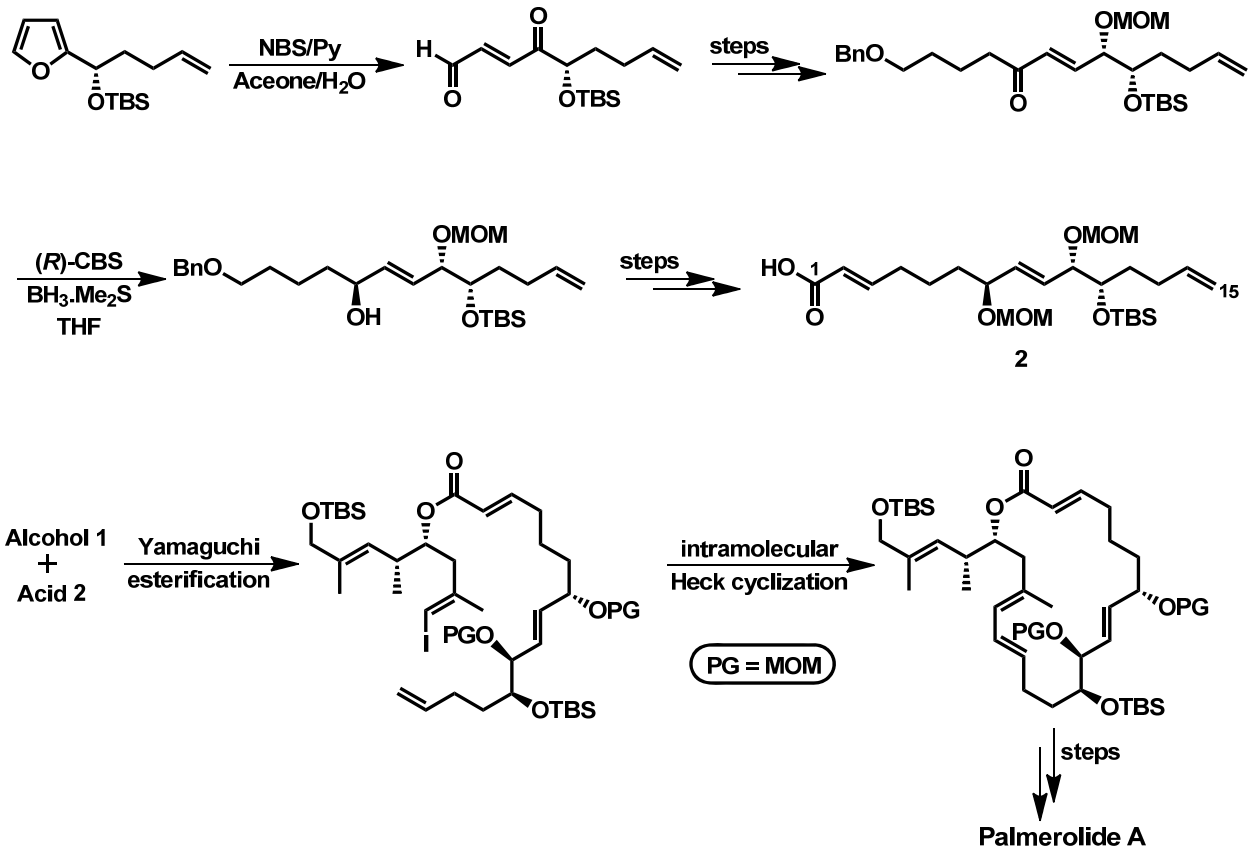
First chapter of the thesis describes the formal total synthesis of bioactive marine macrolide palmerolide A. Palmerolide A was isolated by Baker and co-workers from an Antarctic tunicate *Synoicum adareanum*. Palmerolide A is a 20-membered macrolactone containing five chiral centers and seven unsaturations. Palmerolide A was found to be potent and selectively cytotoxic against human melanoma cancer cell lines and was also shown to inhibit vacuolar V-ATPase.



In section A, enantioselective formal total synthesis of palmerolide A is described. Key steps in the synthesis involve Jung non-aldol aldol reaction to construct the C16-C23 fragment **1** and oxidation of a chiral furyl carbinol to assemble the C1-C15 fragment **2**.

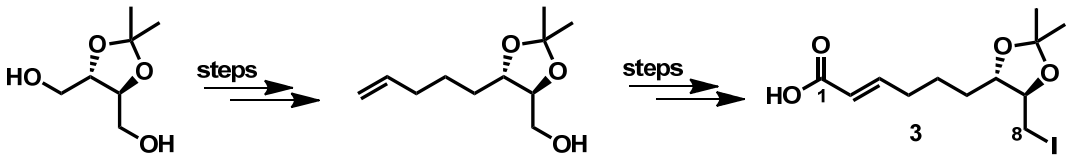


Scheme 1: *Synthesis of C16-C23 fragment of palmerolide A.*

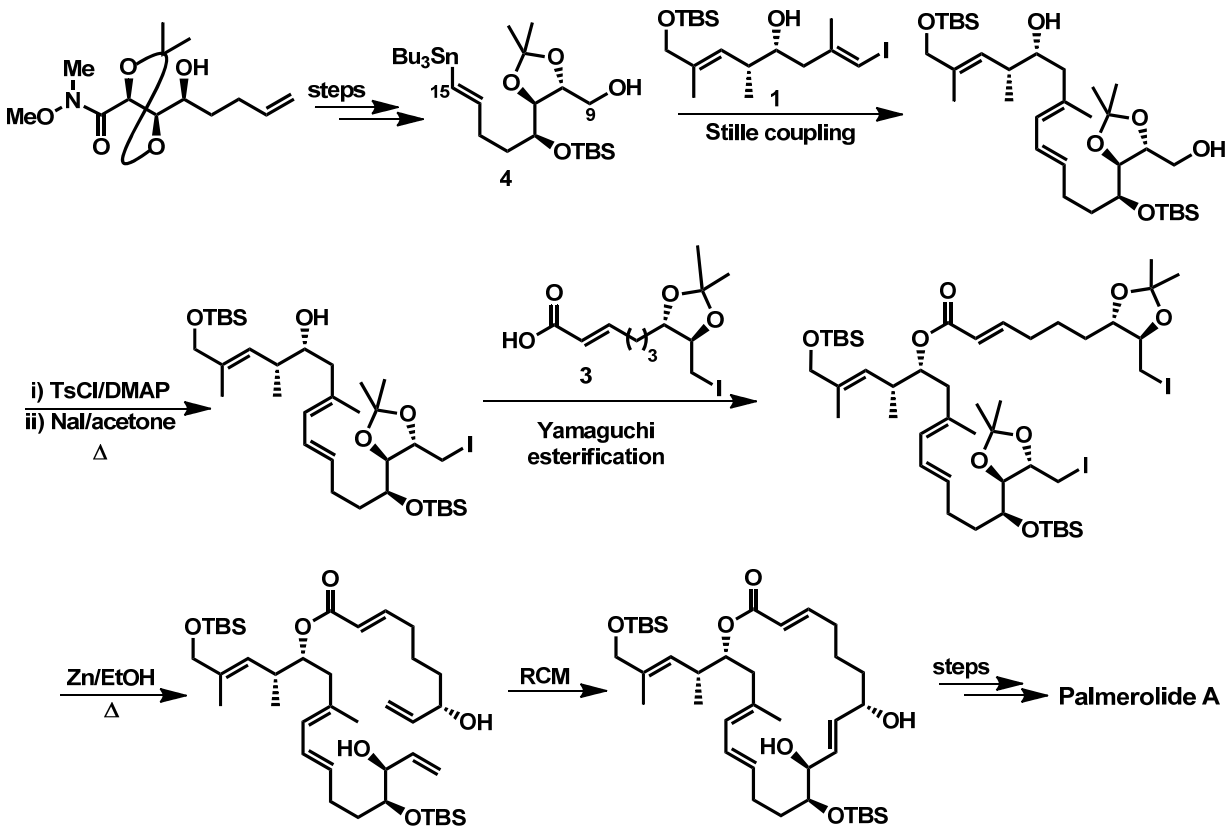


Scheme 2: *Formal total synthesis of palmerolide A.*

In section B, enantiospecific formal total synthesis of palmerolide A is presented from chiral pool tartaric acid. This approach is based on coupling of the three fragments *viz*. C1-C8 enoic acid fragment **3**, C9-C15 vinyl stannane fragment **4** and the C16-C23 vinyl iodide fragment **1**. The C1-C8 enoic acid fragment **3** is synthesized from L-threotol obtained from L-tartaric acid, while synthesis of the C9-C15 fragment **4** involved the elaboration of a γ-hydroxy amide derived from the *bis*-Weinreb amide of tartaric acid. Stille coupling of the vinyl iodide **1** obtained by Jung non-aldol aldol process with the vinyl stannane **4** delivered the C9-C23 unit. Esterification of this unit with the enoic acid **3** followed by zinc mediated Boord olefination and RCM furnished the macrolactone which is further elaborated to palmerolide A.

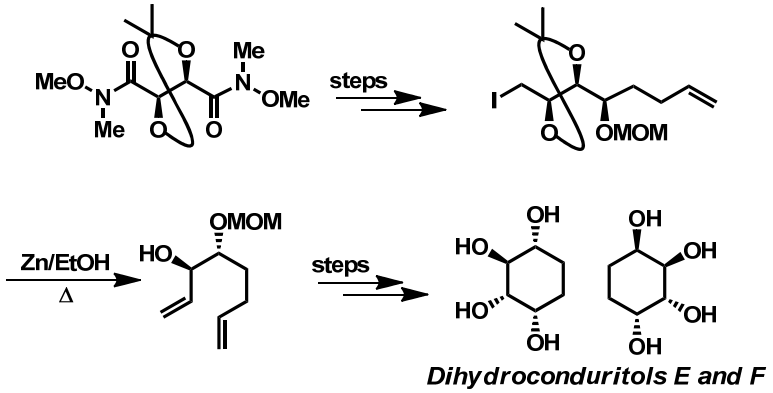


Scheme 3: *Synthesis of C1-C8 fragment of palmerolide A.*



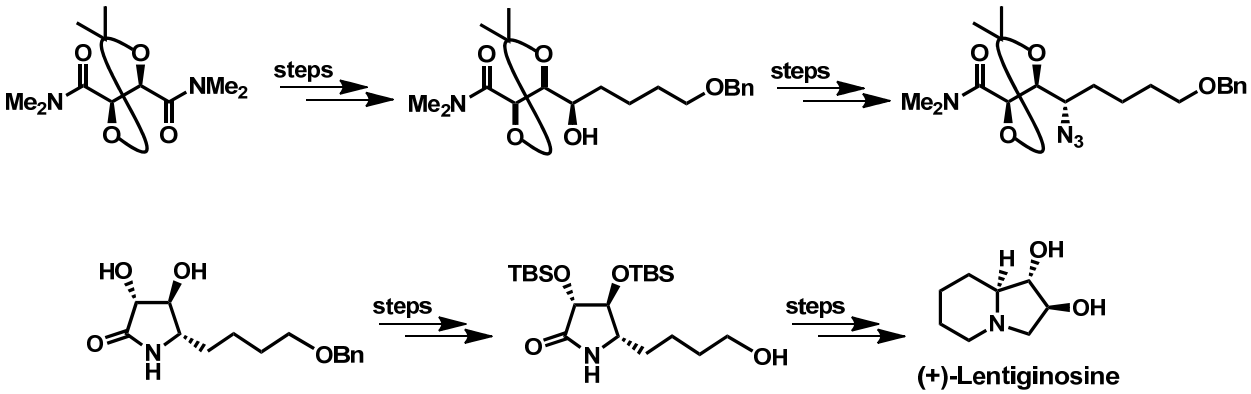
Scheme 4: *Enantiospecific formal total synthesis of palmerolide A.*

Section A of the second chapter deals with the enantiospecific synthesis of dihydro-conduritols E and F from tartaric acid. Conduritols are 1,2,3,4-cyclohex-5-ene tetrols and are shown to be inhibitors of glycosidase. A number of derivatives of conduritols were found to possess various biological activities. Enantiospecific synthesis of dihydroconduritol E and F is accomplished from tartaric acid employing the Boord type fragmentation and ring closing metathesis as the key steps.



Scheme 5: *Enantiospecific synthesis of dihydroconduritols E and F.*

Section B of the second chapter describes the enantiospecific total synthesis of (+)-lentiginosine. Lentiginosine is a dihydroxylated indolizidine alkaloid isolated from leaves of the plant *Astragalus lentiginosus.* Lentiginosine is the most powerful and competitive inhibitor (IC_{50} 5μg/mL) of amyloglucosidase known so far. Key transformation in the synthesis include the *in situ* reduction and cyclization of a dihydroxyazide derived from the γ-hydroxy amide prepared from tartaric acid amide.



Scheme 6: *Enantiospecific total synthesis of (+)-lentiginosine.*